

201-14975A

1-Naphthalenamine, N-phenyl-

CAS # 90-30-2

HPV Test plan

Bayer CropScience LP

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Executive Summary

Bayer CropScience LP (Bayer) hereby submits for review and public comment their test plan for 1-Naphthalenamine, N-phenyl- (N-Phenyl-alpha-Naphthylamine, CAS# 90-30-2) under the Environmental Protection Agency's High Production Volume (HPV) Chemical Challenge Program.

<u>IUPAC Name</u>	<u>Common Name</u>	<u>CAS#</u>
1-Naphthalenamine, N-phenyl-	PANA	90-30-2

PANA is used in jet engine lubricants, both for commercial and military uses. It is also used in turbine oils and miscellaneous lubricants and greases. Small quantities are used to make polymers which are then used in lubricants, and for consumption into rubber industry.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, Bayer has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. Existing data indicates that this chemical is of high concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), low concern for skin and eye irritation, and low concern for acute mammalian toxicity. There were no fertility or developmental studies found, but there is a repeated dose, carcinogenicity study in mice demonstrating lung and kidney tumors. PANA does contain trace amounts of 2-naphthylamine (Beta-naphthylamine, CAS# 91-59-8) which has been given a carcinogenicity designation of "A1-Confirmed human carcinogen" by the American Conference of Governmental Industrial Hygienists (ACGIH). Since exposure is controlled to avoid the risk of carcinogenicity, additional animal testing would not provide useful or relevant data for risk assessment. No additional testing of PANA is proposed for purposes of the HPV Program.

Data Review

Physicochemical properties:

The properties of PANA were available from internal studies and Chemical Dictionary Handbooks. PANA is solid at ambient temperatures and has a melting point of 62-63°C and boiling point of 226°C @ 20hPa. Vapor pressure is less than 0.1 hPa at temperatures from 20 -123°C. The measured octanol/water partition coefficient is 4.28 and PANA is of very low solubility in water (3 mg/l at 20 °C). Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Environmental Fate:

Photodegradation of PANA was measured at 79% degradation after 12 minute(s). Fugacity modeling demonstrates partitioning to the soil (66.3%) and water (27.7%) compartments. There is monitoring data showing ppb levels in manufacturing effluent and low levels in river sediment. Aerobic biodegradation testing demonstrated that PANA did not biodegrade after 28 days under test conditions. A water stability study demonstrated that PANA, in aqueous solution, was eliminated by 48- 55% within 34 days. Several bioaccumulation studies have also been performed using PANA. The BCF in *Cyprinus carpio* (56 days) was 427-2730 (at 0.1 mg/l) and 889-2490 (at 0.01 mg/l). In *Lepomis macrochirus* (10 days at 0.03 mg/l), the BCF based on total 14C residues were 1111 for whole fish, 627 for edible fish and 3820 for viscera. Data is available for all endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Ecotoxicology:

Several aquatic studies have been done. LC₅₀ results of 7.9 mg/l (48 hr, *Oryzias latipes*) and 0.47 mg/l (8 day, *Lepomis macrochirus*) were demonstrated in two of the studies. An EC₅₀ of 0.68 mg/l (48 hr, *Daphnia*) and a chronic invertebrate EC₅₀ of 0.06mg/l (21 day, *Daphnia*) indicate that PANA is toxic to aquatic organisms. Since PANA is toxic to the aquatic environment, acute toxicity to Algae would not supply useful or relevant data for risk assessment. No additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

Mammalian Toxicology:

Toxicity studies in animals show that PANA is of low acute toxicity by the oral and dermal routes of exposure: oral LD₅₀ >5000 mg/kg (male and female rat) and dermal LD₅₀ > 5000 mg/kg (rabbit). (See Table 1 and IUCLID document for more detail).

There are many studies testing the mutagenicity of PANA. There are bacterial gene mutation assays using *Salmonella typhimurium*, *Escherichia coli* and *Saccharomyces cerevisiae*, all with negative results. There are *in vitro* Mammalian Cytogenetic assays using Chinese hamster ovary (CHO) cells and Chinese hamster lung cells, both demonstrating negative results. There is also a Sister chromatid exchange assay in CHO cells and an "Unscheduled DNA synthesis" assay using WI-38 cells, both with ambiguous results. However an *in vivo* Dominant lethal assay in male mice demonstrated a negative result. Data is available for the mutagenicity endpoints, no additional testing is proposed for purposes of the HPV Program (See Table 1 and IUCLID document).

A repeated oral dose study in dogs for 36-42 months demonstrated a NOAEL of 290 mg/kg body weight. There were no fertility or developmental studies found. PANA contains trace amounts of an impurity known to be carcinogenic. Since exposure is controlled to avoid the risk of carcinogenicity, additional animal testing would not provide useful or relevant data for risk assessment. For that reason no testing is proposed for purposes of the HPV Program. (See Table 1 and IUCLID document).

"Beyond SIDS" Endpoints:

Studies have been performed with PANA to investigate skin and eye irritation and were found to be slightly irritating to the skin and non-irritating to the eyes of rabbits. PANA was found to be a dermal sensitizer in guineas pigs.

An oral dose carcinogenicity study has been performed on dogs for 36-42 months with negative results. There is also a carcinogenicity study on mice using sub-cutaneous exposure. Exposure of 262 -295 days showed lung and kidney tumors. However, a critical evaluation by European governing bodies has concluded that there is not sufficient evidence to classify PANA as a carcinogen. (See Table 2 and IUCLID document).

Exposure considerations

During the processing, PANA is a liquid with a relatively low vapor pressure and is handled in a closed system. There are minimal exposure concerns. Employees wear long sleeved shirts, chemical-resistant gloves when appropriate, and safety glasses.

During the drumming of PANA, drums are filled in a ventilated enclosure, and again there are minimal exposure concerns. Employees wear long sleeved shirts, chemical-resistant gloves when appropriate, and safety glasses.

PANA drums are processed so the material can be placed in bags by a third party. Employees at the location utilize respiratory and skin protection to ensure that potential exposures are minimized. Therefore during processing and packaging, with engineering controls and personal protection equipment, exposure is negligible.

Due to the fact that PANA is a small quantity component in formulations used by downstream customers, it is believed that all potential exposures would also be negligible.

Conclusion

Existing data indicates that this chemical is of high concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POP), low concern for skin and eye irritation, and low concern for acute mammalian toxicity. There were no fertility or developmental studies found, but there is a repeated dose, carcinogenicity study in mice demonstrating lung and kidney tumors. PANA does contain trace amounts of 2-naphthylamine (Beta-naphthylamine, CAS# 91-59-8) which has been given a carcinogenicity designation of "A1-Confirmed human carcinogen" by the American Conference of Governmental Industrial Hygienists (ACGIH). Since exposure is controlled to avoid the risk of carcinogenicity, additional animal testing would not provide useful or relevant data for risk assessment. No additional testing of PANA is proposed for purposes of the HPV Program.

Table 1. Available data for PANA (CAS# 66346-01-8)

Endpoint	PANA
Physical-Chemical Data	
Molecular weight	219.29
Physical state	solid
Melting Point	62-63 °C
Boiling Point	226 °C @ 20 hPa
Vapor Pressure	< 0.1 hPa
Partition Coefficient (logP _{ow})	4.28
Water Solubility	3 mg/l at 20 °C
Environmental Fate	
Photodegradation	T ½ = < 12 minutes
Fugacity (distribution)	Air: .05 % Water: 27.7% Soil: 66.3 % Sediment: 5.9 %
Biodegradability	0 % after 28 day(s)
Water Stability	48 - 55 % after 34 day(s)
Ecotoxicology	
Acute Fish Toxicity 48hrs LC ₅₀	7.9 mg/l (<i>Oryzias latipes</i>)
Acute Invertebrate Toxicity 48 hrs EC ₅₀	0.68 mg/l (<i>Daphnia magna</i>)
Algal Toxicity 96 hrs LC ₅₀	No data
Mammalian Toxicology	
Acute Toxicity	LD ₅₀ > 5000 mg/kg bw (oral, male/female rats) LD ₅₀ > 5000 mg/kg bw (dermal, rabbit)
Mutagenicity	Ames = negative
Chromosome Aberration	Cytogenetic assay = negative (CHO cells and CHL cells) Dominant lethal = negative (<i>in vivo</i> , mouse)
Repeated Dose Toxicity	NOAEL = 290 mg/kg bw (oral, dog, 36-42 months)
Reproductive Toxicity	No data
Developmental Toxicity	No data

* Robust summaries and References can be found in the IUCLID document.

Table 2. “Beyond SIDS” data for PANA (CAS# 66346-01-8)

Endpoint	PANA
Ecotoxicology	
Sub-acute Fish Toxicity 8 days LC ₅₀	0.46 - 0.48 mg/l (<i>Lepomis macrochirus</i>) 0.3 mg/l (<i>Oncorhynchus mykiss</i>)
Chronic Invertebrate Toxicity 21 days EC ₅₀	0.06 mg/l (<i>Daphnia magna</i>)
Mammalian Toxicology	
Skin Irritation	Slightly irritating (rabbit)
Eye Irritation	Not irritating (rabbit)
Sensitization	Sensitizing (guinea pig)
Carcinogenicity	Negative (oral, dog, 36-42 months) Lung and kidney tumors but no dose response (sub-cutaneous, mouse)

* Robust summaries and References can be found in the IUCLID document.

Table 3. Test Plan for PANA (CAS# 66346-01-8)

Endpoint	Data Availability	Acceptable	Planned testing
Physical-Chemical Data			
Melting Point	✓	✓	
Boiling Point	✓	✓	
Vapor Pressure	✓	✓	
Partition Coefficient (logP _{ow})	✓	✓	
Water Solubility	✓	✓	
Environmental Fate			
Photodegradation	✓	✓	
Fugacity	✓	✓	
Biodegradability	✓	✓	
Water Stability	✓	✓	
Ecotoxicology			
Acute Fish Toxicity	✓	✓	
Acute Invertebrate Toxicity	✓	✓	
Algal Toxicity			Derogation statement
Mammalian Toxicology			
Acute Toxicity	✓	✓	
Mutagenicity	✓	✓	
Chromosome Aberration	✓	✓	
Repeated Dose Toxicity	✓	✓	
Reproductive Toxicity			Derogation statement
Developmental Toxicity			Derogation statement

✓ = data available and considered adequate.